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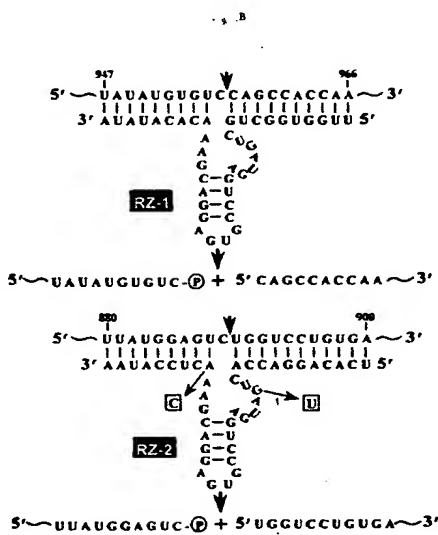
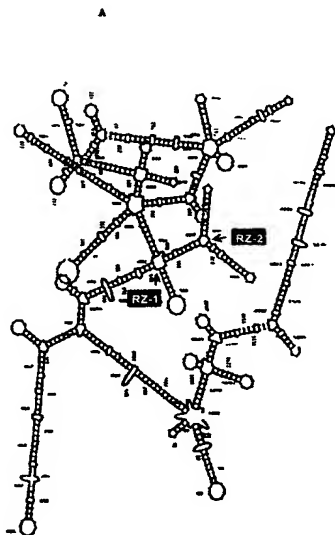
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[Continued on next page]

(54) Title: **ESTROGEN RECEPTOR SITE-SPECIFIC RIBOZYMES AND USES THEREOF FOR ESTROGEN DEPENDENT TUMORS**



(57) Abstract: Highly specific hammerhead ribozymes are provided that human target estrogen receptor mRNA. These ribozymes, designated RZ1 through RZ7 provide predictable mRNA cleavage products. Methods for inhibiting estrogen-dependent tumor growth, such as that characteristic of breast cancer, are also provided employing these ribozymes. One or both of the ribozymes may be used together or separately with equal efficiency. The ribozymes possess a sequence region with a catalytic core that provide the attributed catalytic activity to these ribozymes.

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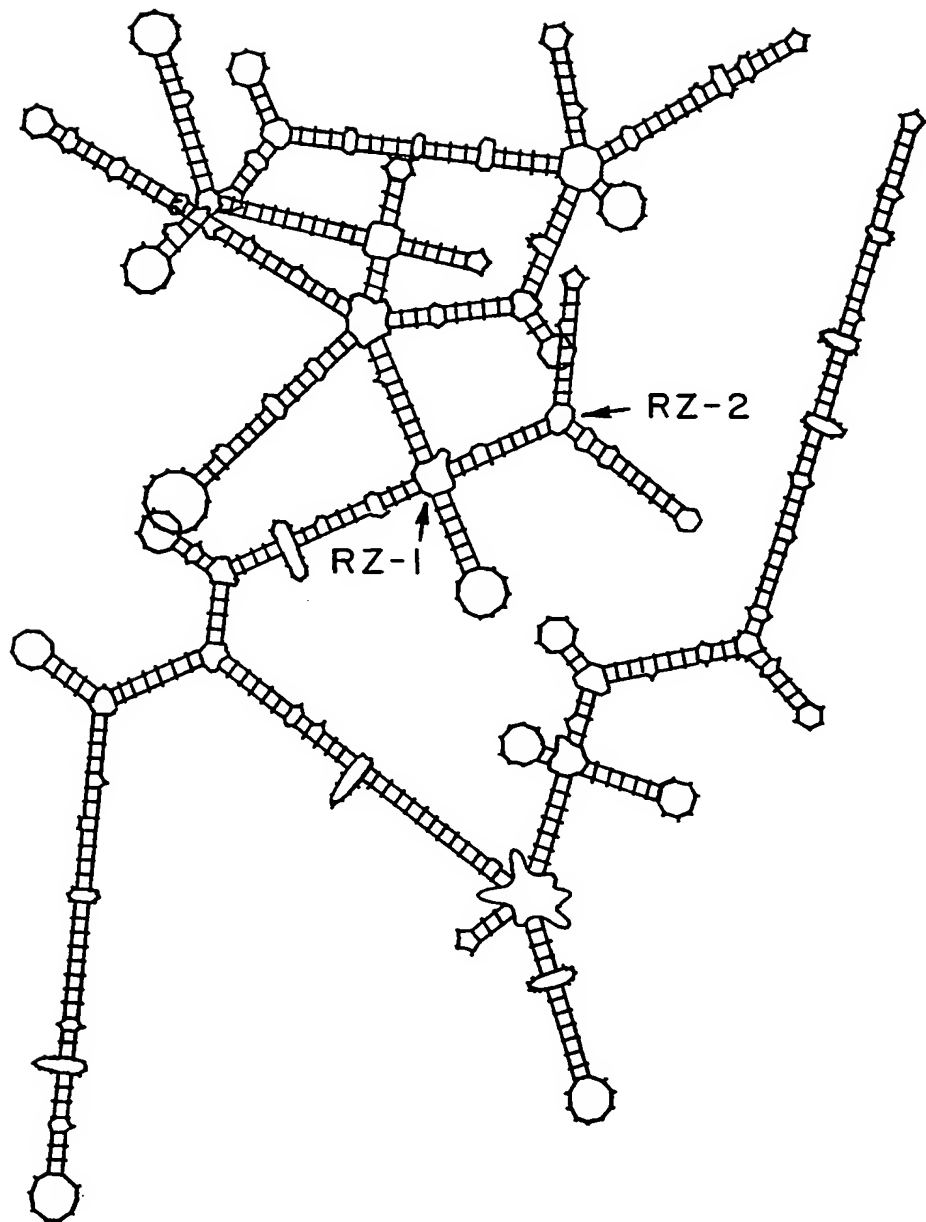


FIG. 1A

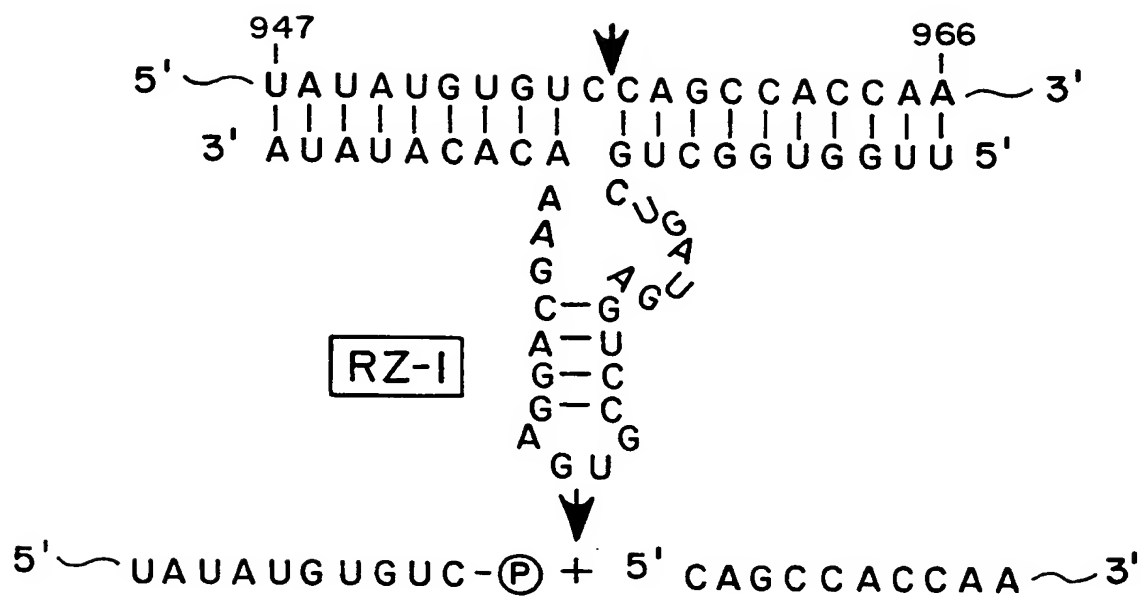


FIG. 1B

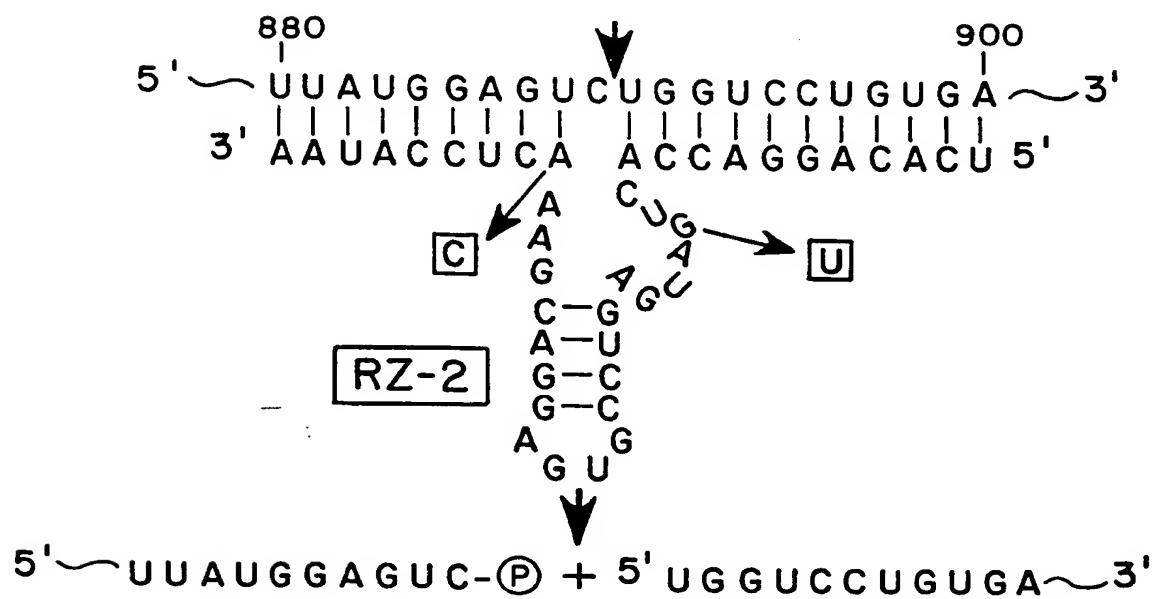
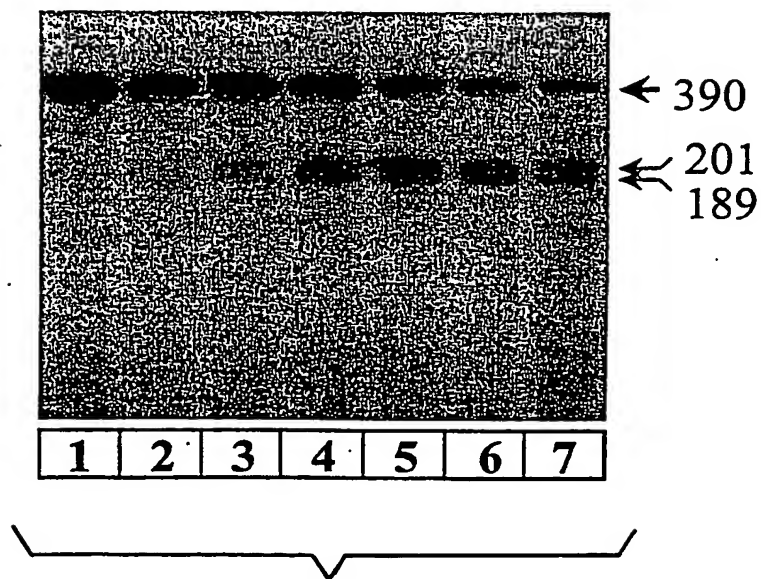
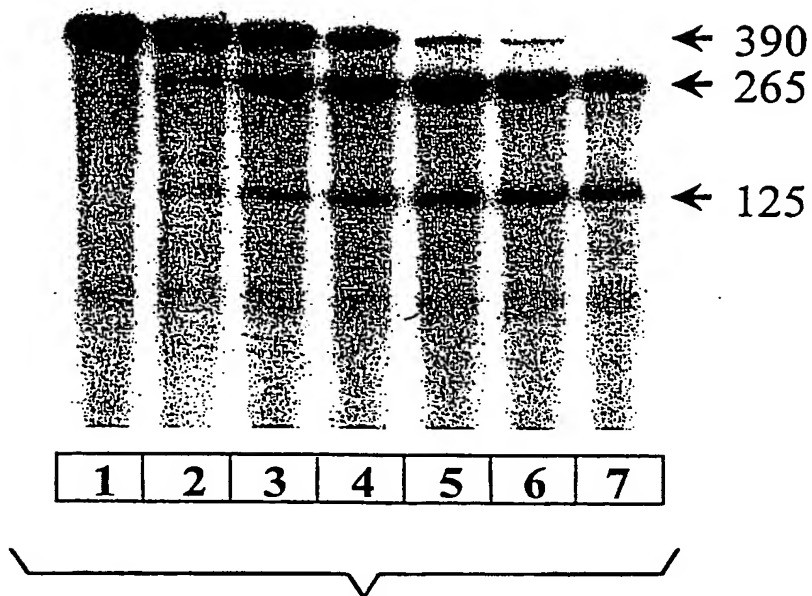


FIG. 1C



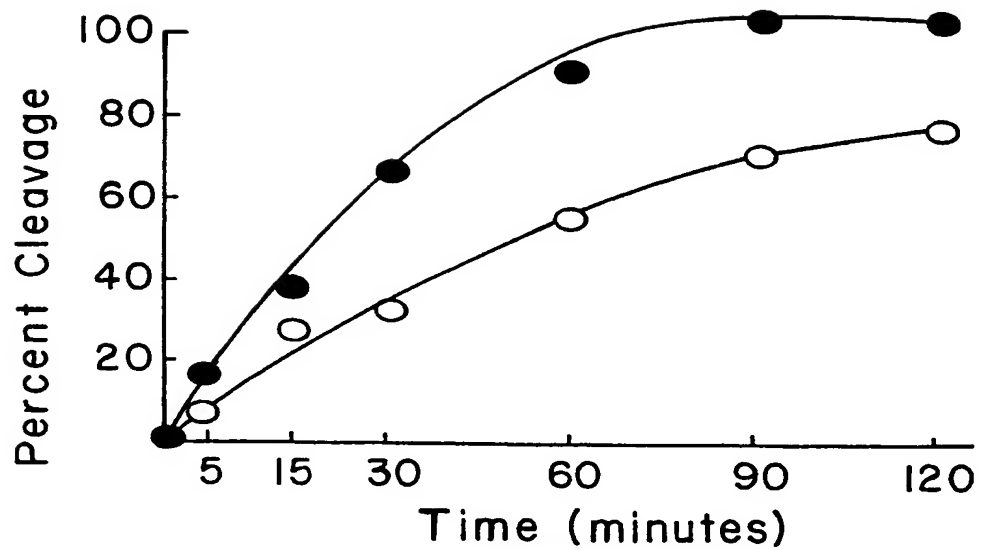


FIG. 2C

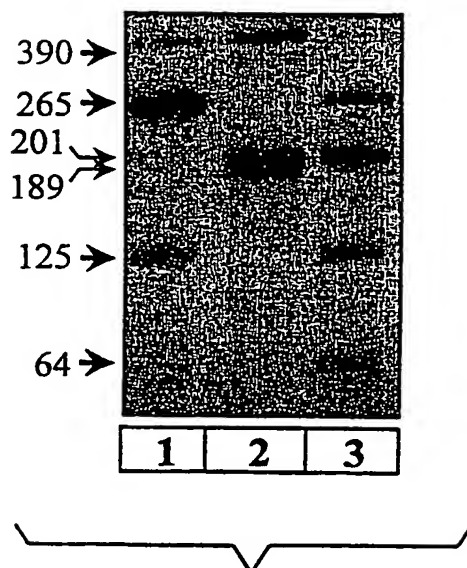


FIG. 2D

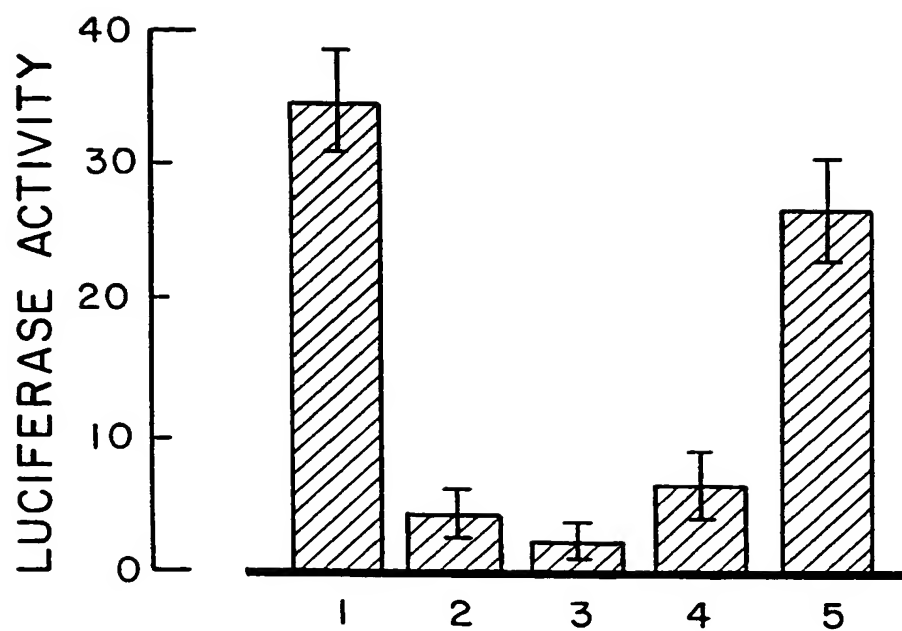


FIG. 3A

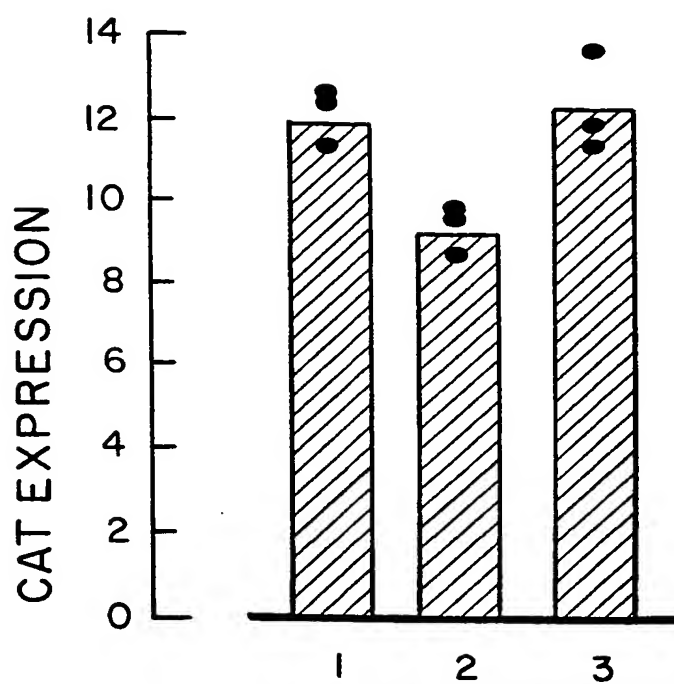
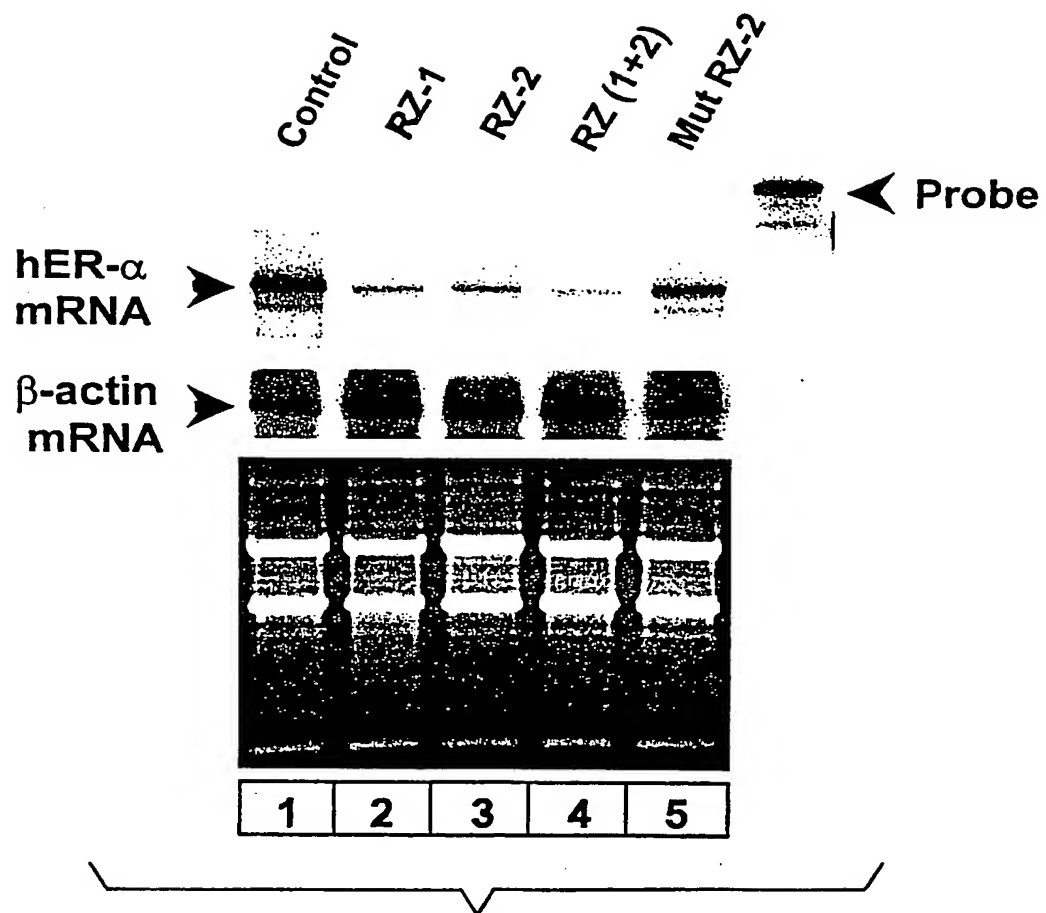


FIG. 3B



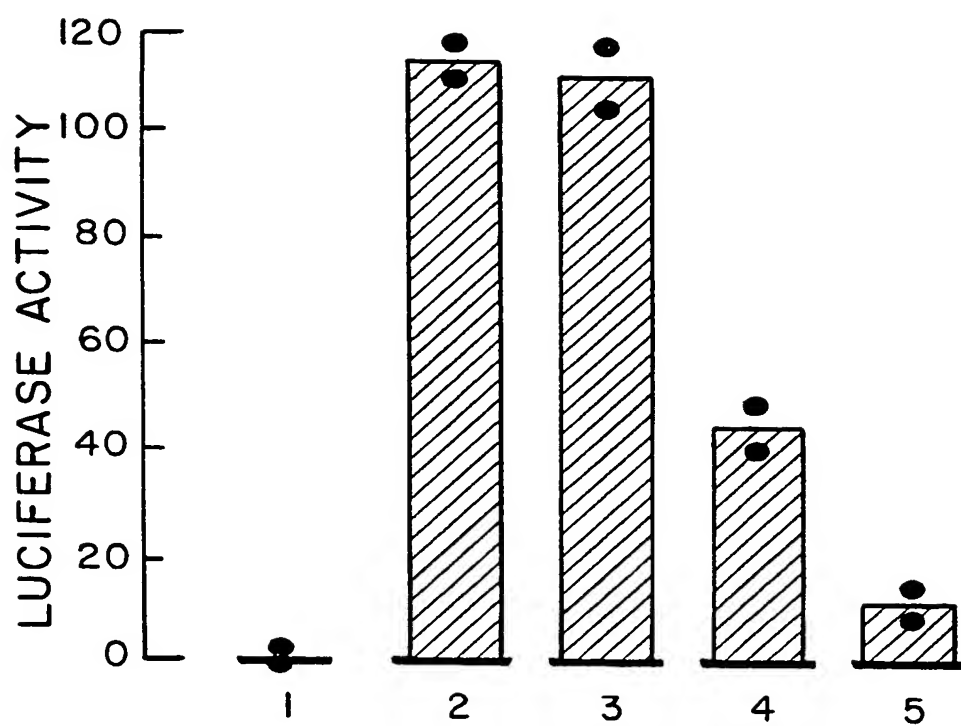
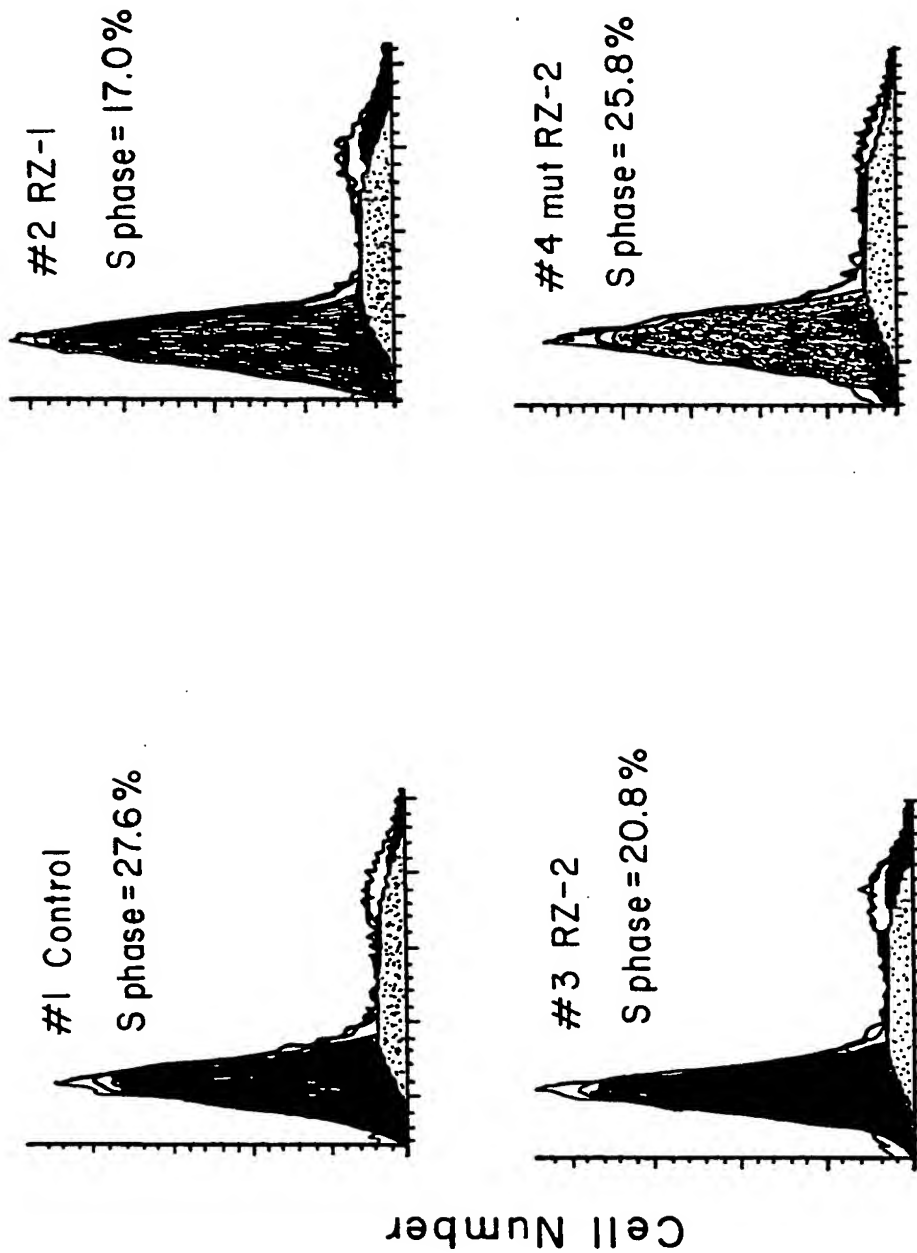


FIG. 5



Relative PI Fluorescence

FIG. 6

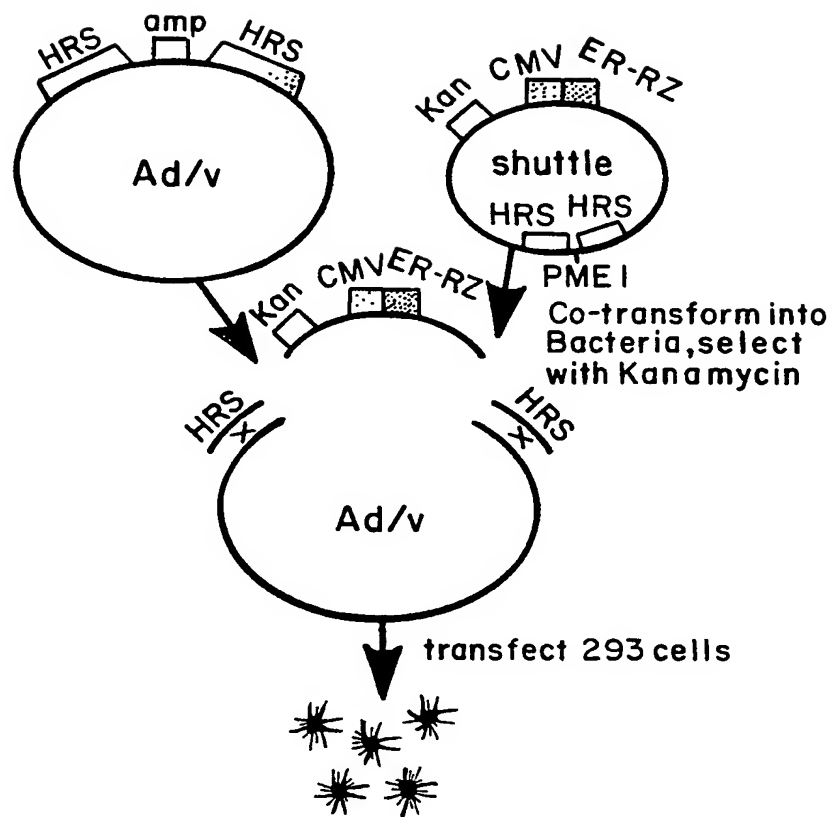
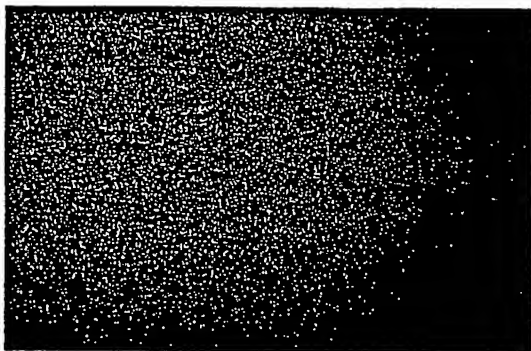
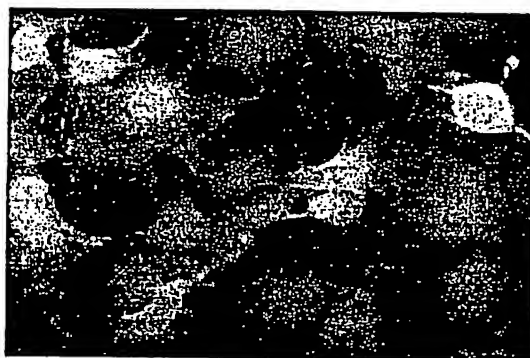


FIG. 7



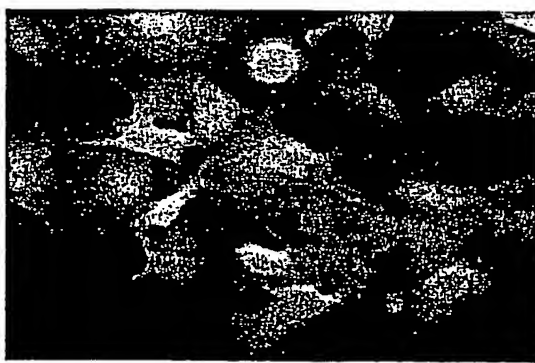
Control cells

FIG. 8A



Ad/v-Rz 2 infected cells

FIG. 8B



Ad/v-Rz 2-M infected cells

FIG. 8C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15243

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/44; 435/6, 91.1, 91.31, 91.5, 455, 366, 375; 536/ 23.1, 24.5, 25.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Dialog, West

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KLEFSTROM et al. C-Myc induces cellular susceptibility to the cytotoxic action of TNF-alpha. The EMBO Journal. 1994, Vol. 13, No. 22, pp. 5442-5450, entire text, especially section entitled :Inhibition of TNF and cMyc-induced apoptosis by Bcl2 and MnSOD", pages 5444-5445.	1-22
A	TURLEY et al. Vitamin E succinate induces Fas-mediated apoptosis in estrogen receptor-negative human breast cancer cells. Cancer Research. 1997, Vol. 57, pp 881-890, see especially last paragraph of intro on page 881 and discussion on pages 887-888.	1-22

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15243

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 99/54459 A2 (RIBOZYME PHARMACEUTICALS, INC.) 28 October 1999 (28.10.99), page 23, line 29-page 27, line 17 and figure 17).	1, 6
Y	MILNER et al. Selecting effective antisense reagents on combinatorial oligonucleotide arrays. Nature Biotech., 1997, Vol. 15, pp 537-541, see entire text.	1-22
Y	JAMES, W. Towards gene-inhibition therapy: a review of progress and prospects in the field of antiviral antisense nucleic acids ribozymes. Antiviral Chem. and Chemotherapy, 1991, Vol. 2, No. 4, pp 191-214, see especially pages 197-198.	1-22

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